STUDIES IN THE MONOCYCLIC TERPENE SERIES

I. THE RESOLUTION OF PHELLANDRIC ACID

II. THE ISOPROPENYL-ISOPROPYLIDENE REARRANGEMENT

III. INVESTIGATIONS OF THE STRUCTURE OF ARTEMISOL

BY

ROBERT EDWARD BERRY

B.S., Brown University, 1944
M.S., University of Illinois, 1947

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
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PART ONE

THE RESOLUTION OF PHELLANDRIC ACID

Introduction

dl-Phellandral has recently been synthesized (1). As the naturally occurring aldehyde has been obtained in both optically active forms it would be of interest and serve as an additional proof of structure to resolve the synthetic mixture and compare the properties of the resolved compound with those of the naturally occurring compound. Both isomers of the naturally occurring aldehyde have been oxidized in an unequivocal manner to the corresponding optically active acids. The resolution of *dl*-phellandric acid, an intermediate in the synthesis of *dl*-phellandral, would therefore be as conclusive as the resolution of *dl*-phellandral itself. In the present work the resolution of *dl*-phellandric acid has been accomplished.

Discussion Of Results

dl-Phellandric acid forms salts with many of the common basic resolving agents, but these salts show only very slight changes in optical purity upon recrystallization from the solvents which were used.

l-Phellandric acid was obtained in a partially pure state by repeated recrystallization of the *d*-α-phenylethylamine salt from a mixture of petroleum ether and *n*-butyl alcohol.

d-Phellandric acid was obtained in an optically pure state by recrystallizing the quinine salt from a mixture of petroleum ether and *n*-butyl alcohol until constant rotation was obtained, hydrolyzing the partially purified salt, forming the *l*-α-phenylethylamine salt from the partially purified acid, recrystallizing this salt from a mixture of petroleum ether and *n*-butyl alcohol until constant rotation was again obtained, and hydrolyzing this optically pure salt to obtain the optically pure dextro-

rotatory acid. The physical constants of this acid agreed with those of the acid obtained from the naturally occurring aldehyde within the limits of experimental error.

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PART TWO

THE ISOPROPENYL-ISOPROPYLIDENE REARRANGEMENT

Introduction

Many terpenes contain either the isopropenyl or the isopropylidene group. The simpler terpenes are usually oils which frequently consist of a mixture of the isopropenyl and the isopropylidene forms in varying proportions. These mixtures, and even some of their solid derivatives, appear to be quite homogenous. Synthetic compounds, presumably containing but one of these forms, have also been found to be mixtures upon analysis. Oils consisting primarily of one form have been found to be easily convertible to a mixture in which the other form predominates. The interrelationship between these two forms has been one of the perplexing problems encountered by terpene chemists (1) (2).

Recently 4-isopropylcyclohexanone has been used as a starting material in a successful synthesis of phellandral. It has been proposed that this synthesis be extended to perillaldehyde using 4-isopropenylcyclohexanone as a starting material. In the present work the isopropenyl-isopropylidene rearrangement was studied in a sample compound of the monocyclic terpene series as a preliminary step to syntheses involving compounds of the 4-isopropenylcyclohexanone type.

Discussion Of Results

The model compound chosen for this investigation was 8(9)-*p*-methane. It had been synthesized previously by several methods from which products of questionable purity had been obtained. To obtain a product of the desired purity a new synthesis was employed involving the series: 4-methylcyclohexanone, ethyl α-(4-methyl-1-hydroxycyclohexyl)-propionate, ethyl α-(4-methyl-1-cyclohexenyl)-propionate, 9-*p*-menthanol, 9-*p*-menthanol acetate and 8(9)-*p*-menthene. Ozonolysis of this product showed that no isomerization to 4(8)-*p*-menthene had taken place in the final step.

Prior to isomerization experiments a search was made to determine the best method of analyzing for the position of the double bond. The infrared method based upon the work of Thompson and Whiffen (2) proved to be the most suitable. These authors pointed out that a compound of the type 8(9)-*p*-menthene would have a very strong absorption band in the neighborhood of 890 cm.$^{-1}$, while none of the possible isomerization products would absorb in that region. This was found to be true in the case of 8(9)-*p*-methene by preparing pure samples of 3-*p*-methene and 4(8)-*p*-menthene, and comparing the absorption spectra of these compounds with that of 8(9)-*p*-menthene.

Samples of 8(9)-*p*-menthene were subjected to various conditions which might be encountered in the proposed synthesis of perillaldehyde and to conditions known to promote isomerization. The double bond was found to be stable under basic conditions and to be fairly mobile under acidic conditions. It was stable under all conditions which were tested in connection with the proposed synthesis of perillaldehyde.

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PART THREE

INVESTIGATIONS OF THE STRUCTURE OF ARTEMISOL

Introduction

Artemisol is an alcohol reported by Kinney, Jackson, DeMytt and Harris (1) to occur in the oil of Artemisia tridentata (American sage brush). They found that it could absorb one mole of hydrogen to give 9-*p*-menthanol, but they did not determine the nature of the unsaturation. There are six possible monoölefinic isomeric alcohols differing only in the position of the double bond which could be hydrogenated to give 9-*p*-menthanol. Two of these isomers have been synthesized in the present work.

Discussion Of Results

Ethyl α-(4-methyl-1-cyclohexene)-propionate was reduced with lithium aluminum hydride to give 3-*p*-menthene-9-ol, an alcohol with the same carbon structure and same empirical formula as artemisol.

The second alcohol, 4(8)-*p*-menthene-9-ol, was prepared by reducing α-(4-methylcyclohexylidene)-propionic acid with lithium aluminum hydride.

The determination of whether either of these alcohols is identical with artemisol must await the formation of a solid derivative of that compound. No such solid derivative has as yet been reported.

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VITA

The author was born in Lynn, Massachusetts, on March 22, 1923. He attended the public schools of Milwaukee, Wisconsin, and Cranston, Rhode Island, and graduated from Cranston High School in June, 1941. In the fall of that year, he entered Brown University where he remained until being ordered to active service in the United States Navy in March, 1944. He received the degree of Bachelor of Science in Chemistry in October, 1944. He was released to inactive duty in the navy in June 1946. In the fall of 1946, he enrolled in the Graduate College of the University of Illinois where he held a teaching assistantship in the inorganic division until June, 1948. He held a University Fellowship from September, 1948, until June, 1949. In June, 1947, he received the degree of Master of Science from the University of Illinois.

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